	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L2	3763	pentagastrin or gastrin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:06			0
2	BRS	L3	1277	proton adj pump	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:09			0
3	BRS	L4	993	3 same inhibit$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:09			0
4	BRS	L5	1773	rabeprazole or omeprazole or lansoprazole or pantoprazole	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:08			0
5	BRS	L6	91	2 same (4 or 5)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:10			0
6	BRS	L7	82	gastric adj proton adj pump	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:09			0
7	BRS	L8	72	7 same inhibit$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:09			0
8	BRS	L9	29	2 same (4 or 5) same (combin$5 or conjunct$3 or adjunct$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:40			0
9	BRS	L10	1	2 same 8 same (combin$5 or conjunct$3 or adjunct$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:42			0
10	BRS	L11	3707	gastric adj acid adj secretion	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:41			0
11	BRS	L12	925	(zollinger or ellison) adj syndrome	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:41			0

	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
12	BRS	L13	3355	(gastroesophageal adj reflux adj disease) or (peptic adj ulcer adj disease) or (atrophic adj gastritis) or esophagitis or (idiopathic adj gastric adj acid adj hypersecretion)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:42			0
13	BRS	L14	41	6 same (11 or 12 or 13)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:42			0
14	BRS	L17	7	14 same (combin$5 or conjunct$3 or adjunct$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:45			0
15	BRS	L18	124712	antibiotic or penicillin or tetracycline or macrolide or cephalosporin or fluoroguinone	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:47			0
16	BRS	L19	24	(8 or 9 or 14) same 18	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:48			0
17	BRS	L20	0	pisegna adj joseph.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:49			0
18	BRS	L21	2	wank adj stephen.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/08/14 07:49			0

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FILE 'AGRICOLA' ENTERED AT 08:01:08 ON 14 AUG 2003

=> s pentagastrin or gastrin
L1       83063 PENTAGASTRIN OR GASTRIN

=> s proteon pump
L2           0 PROTEON PUMP

=> s proton pump
L3       28429 PROTON PUMP

=> s l3 (p) inhibit?
L4       17931 L3 (P) INHIBIT?

=> s l1 (p) l4
L5         893 L1 (P) L4

=> s rabeprazole or omerprazole or lansoprazole or pantoprazole
L6       10766 RABEPRAZOLE OR OMERPRAZOLE OR LANSOPRAZOLE OR PANTOPRAZOLE

=> s l1 (p) l6
L7         698 L1 (P) L6

=> s l5 or l7
L8        1268 L5 OR L7

=> s l8 (p) (combinat? or conjunct? or adunct?)
L9          75 L8 (P) (COMBINAT? OR CONJUNCT? OR ADUNCT?)

=> duplicate remove l9
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L9
L10          33 DUPLICATE REMOVE L9 (42 DUPLICATES REMOVED)

=> d l10 1-33 ibib abs

L10  ANSWER 1 OF 33  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2001:247197  CAPLUS
DOCUMENT NUMBER:          134:247252
TITLE:                    Use of pentagastrin to inhibit gastric acid secretion
                          or as a diuretic
INVENTOR(S):              Pisegna, Joseph R.; Wank, Stephen
PATENT ASSIGNEE(S):       The Regents of the University of California, USA
SOURCE:                   PCT Int. Appl., 42 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     --------------    ----  --------       --------------    --------
     WO 2001022985     A1    20010405       WO 2000-US26992   20000928
     WO 2001022985     C2    20020926
         W:  CA, JP
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
PRIORITY APPLN. INFO.:                    US 1999-156491P  P  19990928
```

US 2000-671764 A 20000927

AB ***Pentagastrin*** , when administered in ***conjunction*** with a ***proton*** ***pump*** ***inhibitor*** (PPI), is synergistic with the PPI and significantly increases the efficacy of the PPI in reducing/mitigating excess gastric acid secretion.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2000:284061 BIOSIS
DOCUMENT NUMBER: PREV200000284061
TITLE: Despite of ulcer healing no change in intragastric acidity after successful eradication in duodenal ulcer patients.
AUTHOR(S): Racz, Istvan (1); Szabo, Andrea (1); Pecsi, Gyula (1); Csondes, Mihaly (1); Goda, Maria (1)
CORPORATE SOURCE: (1) Petz Aladar Teaching Hosp, Gyor Hungary
SOURCE: Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 2, pp. AGA A1298. print.
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week San Diego, California, USA May 21-24, 2000 American Gastroenterological Association
. ISSN: 0016-5085.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L10 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:753096 CAPLUS
DOCUMENT NUMBER: 132:452
TITLE: Method for the treatment of gastroesophageal reflux disease using anti- ***gastrin*** immunogenic compn. immunization ***combination*** with H2 antagonist or ***proton*** ***pump*** ***inhibitor***
INVENTOR(S): Gevas, Philip C.; Grimes, Stephen; Karr, Stephen; Michaeli, Dov
PATENT ASSIGNEE(S): Aphton Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959612	A1	19991125	WO 1999-US10734	19990514
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2332774	AA	19991125	CA 1999-2332774	19990514
AU 9940798	A1	19991206	AU 1999-40798	19990514
AU 758955	B2	20030403		
EP 1077716	A1	20010228	EP 1999-924252	19990514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002515448	T2	20020528	JP 2000-549276	19990514
US 2003068326	A1	20030410	US 2002-314057	20021206

PRIORITY APPLN. INFO.:
US 1998-85610P P 19980515
WO 1999-US10734 W 19990514
US 2001-700378 A1 20010301

AB A method for the treatment of gastroesophageal reflux disease comprises a ***combination*** of active immunization with an anti- ***gastrin*** immunogenic compn. with an antagonist which blocks or ***inhibits*** the gastric acid pump activity; or alternatively administering purified anti- ***gastrin*** antibodies with a H2 antagonist or ***proton*** ***pump*** ***inhibitor*** of the gastric acid producing enzyme system.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 33 MEDLINE on STN DUPLICATE
ACCESSION NUMBER: 1999323865 MEDLINE
DOCUMENT NUMBER: 99323865 PubMed ID: 10394031
TITLE: Successful symptomatic management of a patient with Menetrier's disease with long-term antibiotic treatment.
AUTHOR: Raderer M; Oberhuber G; Templ E; Wagner L; Potzi R; Wrba F; Hejna M; Base W
CORPORATE SOURCE: Department of Internal Medicine I, University of Vienna, Austria.
SOURCE: DIGESTION, (1999 Jul-Aug) 60 (4) 358-62.
Journal code: 0150472. ISSN: 0012-2823.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990819

AB We present the case of a 79-year-old female patient with criteria typical for Menetrier's disease, i.e. enlargement of the gastric folds due to foveolar hyperplasia associated with severe protein-loss along with epigastric pain, nausea, vomiting and weight loss. ***Gastrin*** levels were within the normal range, but elevated Helicobacter pylori antibody titers (83 microg/ml) were indicative of a recent infection. Histologic examination of a gastric polyp, which was removed in toto, revealed the presence of early gastric cancer of the mucosal type. After initiation of antibiotic treatment with clarithromycin (3 x 250 mg/day) and metronidazole (2 x 500 mg/day) in ***combination*** with ***lansoprazole*** (30 mg/day), the patient's condition improved rapidly along with abrogation of protein loss. Under maintenance treatment as indicated above, the patient has been free of symptoms now for a period of more than 2 years. On repetitive endoscopic follow-up, there was no change in gastric mucosa morphology either endoscopically or histologically, and also no evidence of recurrence of a malignant lesion. We conclude that this therapeutic regimen represented an effective alternative to surgical intervention in this patient and should be considered in similar cases.

L10 ANSWER 5 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:324499 BIOSIS
DOCUMENT NUMBER: PREV199900324499
TITLE: Hyperpepsinogenemia in Helicobacter pylori infected subjects may not be due to pepsinogen gene overexpression.
AUTHOR(S): Watanabe, Toru (1); Kishi, Kiyohiko (1); Sawada, Mitsutaka (1); Chiba, Tsutomu
CORPORATE SOURCE: (1) Kyoto Univ Hosp, Kyoto Japan
SOURCE: Gastroenterology, (April, 1999) Vol. 116, No. 4 PART 2, pp. A350.
Meeting Info.: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association Orlando, Florida, USA May 16-19, 1999 American Gastroenterological Association
. ISSN: 0016-5085.
DOCUMENT TYPE: Conference
LANGUAGE: English

L10 ANSWER 6 OF 33 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1998444910 MEDLINE
DOCUMENT NUMBER: 98444910 PubMed ID: 9773926
TITLE: Effect of pirenzepine on gastric endocrine cell kinetics during lansoprazole administration.
AUTHOR: Omura N; Kashiwagi H; Gang C; Omura K; Aoki T
CORPORATE SOURCE: Department of Surgery, The Jikei University School of Medicine, Tokyo, Japan.
SOURCE: JOURNAL OF GASTROENTEROLOGY, (1998 Oct) 33 (5) 634-9.
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981215

AB We studied the effect of pirenzepine on gastric secretion kinetics in rats

in a hypochlorhydric state induced by ***lansoprazole*** , a ***proton*** ***pump*** ***inhibitor*** . Pirenzepine was administered intramuscularly at a dosage of 20 mg/kg twice daily; and lansorprazole, subcutaneously at 50 mg/kg once daily, both every day for 4 weeks. After the 4-week treatment, serum ***gastrin*** and plasma somatostatin levels were determined by radioimmunoassay. In addition, ***gastrin*** cells, somatostatin cells, and enterochromaffin-like cells were immunostained and counted. Serum ***gastrin*** levels were elevated, and ***gastrin*** and enterochromaffin-like cell numbers increased in the group on ***lansoprazole*** alone, compared with these values in the control group (which received distilled water). In the group on the ***lansoprazole*** and pirenzepine ***combination*** , serum ***gastrin*** levels decreased, and ***gastrin*** and enterochromaffin-like cell numbers were significantly decreased, compared with the respective variables in the group on ***lansoprazole*** alone, while the number of somatostatin cells increased in the group on the ***combination*** . Plasma somatostatin levels did not vary significantly in any group. It was thus demonstrated that pirenzepine corrects the abnormal gastric secretion kinetics resulting from treatment with ***lansoprazole*** alone, such as hypergastrinemia and ***gastrin*** and enterochromaffin-like cell hyperplasia.

L10 ANSWER 7 OF 33 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1998332293 MEDLINE
DOCUMENT NUMBER: 98332293 PubMed ID: 9669630
TITLE: Potentiating hypergastrinemic effect by the peroxisome proliferator ciprofibrate and omeprazole in the rat.
AUTHOR: Hammer T A; Sandvik A K; Waldum H L
CORPORATE SOURCE: Dept. of Medicine, Norwegian University of Science and Technology, Trondheim.
SOURCE: SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY, (1998 Jun) 33 (6) 595-9.
Journal code: 0060105. ISSN: 0036-5521.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980925
Last Updated on STN: 19980925
Entered Medline: 19980915
AB BACKGROUND: Profound ***inhibition*** of gastric acid secretion induces enterochromaffin-like (ECL) cell carcinoids due to hypergastrinemia. Peroxisome proliferators also lead to hypergastrinemia and ECL cell carcinoids but without reducing gastric acidity. Since the peroxisome proliferator ciprofibrate is still in use as lipid-reducing agent, and ***proton*** ***pump*** ***inhibitors*** are among the most commonly used drugs, we found it of interest to evaluate both the effect of a ***combination*** of these drugs on serum ***gastrin*** and the expression of ***gastrin*** and somatostatin mRNA in antral mucosa. METHODS: The drugs were given by gastric gavage once daily for 4 weeks to female rats. Blood was drawn by vein puncture before and at the end of the 4-week period for determination of ***gastrin*** by radioimmunoassay. At death the stomachs were removed, the antral mucosa homogenized, and the density of ***gastrin*** and somatostatin mRNA determined by Northern blot, using 32P-labelled probes. RESULTS: Omeprazole dosing increased serum ***gastrin*** 4-fold, ciprofibrate 5-fold, and the ***combination*** 24-fold. Serum ***gastrin*** during ciprofibrate dosing increased gradually, reaching significance after 14 days. Antral ***gastrin*** mRNA density increased similarly to the increase in serum ***gastrin*** , whereas antral somatostatin mRNA tended to be reduced in the omeprazole and increased in the ciprofibrate-dosed rats. CONCLUSION: A potentiating hypergastrinemic effect of the peroxisome proliferator ciprofibrate and the ***inhibitor*** of gastric acid secretion omeprazole is shown, indicating different mechanisms of action.

L10 ANSWER 8 OF 33 MEDLINE on STN
ACCESSION NUMBER: 1999246938 MEDLINE
DOCUMENT NUMBER: 99246938 PubMed ID: 10230323
TITLE: [The significance of Helicobacter pylori in medical science].
De betekenis van Helicobacter pylori in de geneeskunde.
AUTHOR: Tytgat G N
CORPORATE SOURCE: Departement Gastroenterologie en Hepatologie, Universiteit van Amsterdam, Nederland.

SOURCE: VERHANDELINGEN - KONINKLIJKE ACADEMIE VOOR GENEESKUNDE VAN BELGIE, (1998) 60 (6) 521-32; discussion 532-3 Ref: 39
Journal code: 0413210. ISSN: 0302-6469.
PUB. COUNTRY: Belgium
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Dutch
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990525

AB The discovery of Helicobacter pylori as a dominant cause of gastritis is at least revolutionary both with respect to its clinical consequences as to its contribution to fundamental basic science. The velocity with which basic and clinical experience was accumulated in the H. pylori field has been unsurpassed in medicine. The organism is highly complex and can be divided in two subclasses, a more virulent strain containing the socalled 'pathogenicity island' in addition to vacA and IceA1 antigen and an almost commensal-like subtype. The virulent type in particular is associated with severe inflammation and various clinical disease states. The pathogenesis of duodenal ulcer is well understood. The infection is essentially limited to the antrum causing disturbance of the ***gastrin*** homeostasis which is one of the mechanisms leading to enhanced acid production. This constant hyperacidity in the duodenal bulb ultimately leads to development of gastric metaplasia with production of neutral mucus. The latter is essential to allow colonisation with the organism, leading to inflammation, erosion and ultimately ulcer. Curing the infection leads to permanent cure of the ulcer diathesis. The mechanisms that ultimately lead to gastric cancer or gastric Malt lymphoma are less clear. Curing the infection turns out to be more difficult than initially anticipated. Currently the triple therapy (a ***combination*** of a ***proton*** ***pump*** ***inhibitor*** with clarithromycin and either amoxycillin or metronidazole), or bismuth triple therapy or bismuth quadruple therapy (a ***combination*** of a ***proton*** ***pump*** ***inhibitor*** , bismuth, tetracyclin and metronidazole) are most commonly used. Sadly there is a rising frequency of resistance throughout the world against metronidazole and clarithromycin. Finally increasingly H. pylori infection is considered a model for study of fundamental biological problems such as interaction between organism and host, intracellular signalling in case of infection, evolution of inflammation towards atrophy and cancer etc. Equally interesting is the discovery of novel Helicobacters, such as Helicobacter resistance to bile or Helicobacters responsible for intestinal inflammation.

L10 ANSWER 9 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:30433 BIOSIS
DOCUMENT NUMBER: PREV199800030433
TITLE: Effects of enprostil on gastric endocrine secretion during chronic administration of lansoprazole.
AUTHOR(S): Omura, Nobuo (1); Kashiwagi, Hideyuki; Aoki, Teruaki; Omura, Kayoko; Fukuichi, Yasunori
CORPORATE SOURCE: (1) Dep. Surgery II, Jikei Univ. Sch. Med., 3-25-8 Nishishinbashi, Minato-ku, Tokyo 105 Japan
SOURCE: Journal of Gastroenterology, (Dec., 1997) Vol. 32, No. 6, pp. 740-746.
ISSN: 0944-1174.
DOCUMENT TYPE: Article
LANGUAGE: English

AB We investigated changes in the secretory kinetics of gastric endocrine cells related to the administration of lansoprazole, and the effects of enprostil on these altered kinetics. Male Wistar-derived 8-week-old rats were allotted to a control group, a lansoprazole administration group, an enprostil administration group, and a lansoprazole + enprostil administration group. Lansoprazole (30 mg/kg once a day for 4 weeks) and enprostil (10 mug/kg twice a day for 4 weeks) were administered into the gastric lumen with a gastric tube. At this time, blood was collected and immunohistological staining of gastric endocrine cells was conducted to investigate the secretory kinetics. Lansoprazole administration induced hypergastrinemia, increase of gastrin cells, and increase of enterochromaffin-like cells. Enprostil administration induced increase of somatostatin cells. The group administered lansoprazole + enprostil exhibited significant decreases in serum gastrin level, total gastrin cell count, and total enterochromaffin-like cell count, compared with the group administered lansoprazole alone. These findings suggest that enprostil may

ameliorate the alteration in gastric endocrine secretion produced by the chronic administration of lansoprazole.

L10 ANSWER 10 OF 33 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 97349867 MEDLINE
DOCUMENT NUMBER: 97349867 PubMed ID: 9205747
TITLE: Anti-Helicobacter pylori activities of ebrotidine. A review of biochemical and animal experimental studies and data.
AUTHOR: Slomiany B L; Piotrowski J; Slomiany A
CORPORATE SOURCE: Research Center, University of Medicine and Dentistry of New Jersey, Newark, USA.
SOURCE: ARZNEIMITTEL-FORSCHUNG, (1997 Apr) 47 (4A) 475-82. Ref: 64
Journal code: 0372660. ISSN: 0004-4172.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199708
ENTRY DATE: Entered STN: 19970825
Last Updated on STN: 19970825
Entered Medline: 19970813

AB Infection with Helicobacter pylori (H. pylori) is now recognized as a major factor in the pathogenesis of gastric disease, and the successful therapy regimens require a ***combination*** of H2 blockers with gastroprotective and antimicrobial agents. Ebrotidine (N-[(E)-[[2-[[[2-[(diaminomethylene) amino]-4-thiazolyl] methyl]thio]ethyl]amino]methylene]-4-bromo-benzenesulfonamide, CAS 100981-43-9, FI-3542) is the only drug combining acid-suppressant activity with remarkable gastroprotective and anti-H. pylori properties. The drug not only displays a potent anti-H. pylori activity alone, but also exerts a strong potentiating effect on the efficacy of antimicrobial agents commonly used for H. pylori eradication, and the successful ulcer therapy with ebrotidine induces a significant (4-fold) increase in the H. pylori aggregation titer of gastric mucin. Moreover, the drug exhibits a strong inhibitory effect on H. pylori urease activity, the extent of which exceeds that of ranitidine, omeprazole and ***lansoprazole*** . Ebrotidine has also been demonstrated to exert a potent inhibitory action on the enzymatic activities directed towards mucus perimeter of gastric mucosal defense, causing a marked inhibition of H. pylori protease, lipase and phospholipase A2 activities. Another important property of ebrotidine is its ability to efficiently counteract the disruptive effects of H. pylori lipopolysaccharide on the integrity of gastric epithelium. This includes countering the interference by the lipopolysaccharide in mucosal integrin receptor interaction with proteins of extracellular matrix and the reversal of H. pylori disruptive effect on the binding of mucin to its gastric epithelial receptor. Furthermore, most recent data indicate that ebrotidine has the ability to reverse the impairment caused by H. pylori in feedback inhibition of ***gastrin*** release by somatostatin. This activity of ebrotidine apparently stems from the drug's ability to counter the untoward effect of H. pylori on the binding of somatostatin to its specific receptor on the gastric mucosal G-cells. The unique ***combination*** of acid suppressant, gastroprotective and anti-H. pylori activities makes ebrotidine a drug of choice in the treatment of gastric disease caused by H. pylori.

L10 ANSWER 11 OF 33 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97156057 MEDLINE
DOCUMENT NUMBER: 97156057 PubMed ID: 9002534
TITLE: Eradication of Helicobacter pylori in patients with end-stage renal disease under dialysis treatment.
AUTHOR: Tamura H; Tokushima H; Murakawa M; Matsumura O; Itoyama S; Sekine S; Hirose H; Mitarai T; Isoda K
CORPORATE SOURCE: Fourth Department of Internal Medicine, Saitama Medical Center, Kawagoe, Japan.
SOURCE: AMERICAN JOURNAL OF KIDNEY DISEASES, (1997 Jan) 29 (1) 86-90.
Journal code: 8110075. ISSN: 0272-6386.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19970227
Entered Medline: 19970213

AB The efficacy and safety of ***combination*** therapy with amoxicillin, ***lansoprazole*** , and plaunotol for the eradication of Helicobacter pylori in patients on dialysis were evaluated. The study subjects comprised 15 dialysis patients in whom H pylori had been found in the gastric mucosa. The patients were given 500 mg amoxicillin once a day for 3 weeks, 30 mg ***lansoprazole*** once a day for 8 weeks, and 80 mg plaunotol three times a day for 24 weeks. Endoscopy was performed on entry and at 4 and 24 weeks after cessation of amoxicillin. The concentrations of serum ***gastrin*** and gastric juice ammonia also were measured. Fourteen patients completed the treatment protocol, one having dropped out because of nausea and diarrhea. H pylori was eradicated in 11 of the 14 patients 4 weeks after the end of amoxicillin therapy (eradication rate, 78.6%). All but one patient was free of H pylori 24 weeks after the amoxicillin was discontinued. Patients who became negative for H pylori had significantly decreased serum ***gastrin*** and gastric juice ammonia concentrations. Our findings indicate that a ***combination*** of amoxicillin, ***lansoprazole*** , and plaunotol can be used to eradicate H pylori in patients on dialysis.

L10 ANSWER 12 OF 33 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 96426045 MEDLINE
DOCUMENT NUMBER: 96426045 PubMed ID: 8828354
TITLE: Eradication of Helicobacter pylori in patients with end-stage renal disease undergoing dialysis treatment.
AUTHOR: Tokushima H; Tamura H; Matsumura O; Murakawa M; Itakura Y; Itoyama S; Mitarai T; Isoda K
CORPORATE SOURCE: Fourth Department of Internal Medicine, Saitama Medical Center, Saitama Medical School, Japan.
SOURCE: NIPPON JINZO GAKKAI SHI. JAPANESE JOURNAL OF NEPHROLOGY, (1996 Aug) 38 (8) 349-55.
Journal code: 7505731. ISSN: 0385-2385.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970319
AB The aim of the present study was to examine the efficacy and safety of ***combination*** therapy with amoxicillin (AMPC), ***lansoprazole*** , and plaunotol for the eradication of H. pylori in dialysis patients. The subjects consisted of 15 dialysis patients (10 men and 5 women, mean age of 56 +/- 2.4 years) in whom H. pylori was found in the stomach. H. pylori status was evaluated by histology, culture and rapid urease test with biopsy specimens of the gastric mucosa. The patients were treated with AMPC 500 mg once a day for 3 weeks, ***lansoprazole*** 30 mg once a day for 8 weeks and plaunotol 80 mg three times a day for 24 weeks. In addition, the concentrations of serum ***gastrin*** and gastric juice ammonia were measured. Fourteen patients completed the treatment schedule, while one discontinued treatment because of nausea and diarrhea. Among the 14 patients, H. pylori was eradicated in 11 without any side effects (eradication rate 78.6%). Concentrations of gastric juice ammonia and serum ***gastrin*** were reduced significantly in patients who became H. pylori-negative. The present study indicates that ***combination*** therapy with AMPC, ***lansoprazole*** and plaunotol is safe and efficient for the eradication of H. pylori in dialysis patients. The results also suggested that elevated concentrations of gastric juice ammonia and serum ***gastrin*** in dialysis patients can be attributed, at least in part, to H. pylori infection.

L10 ANSWER 13 OF 33 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 96261545 MEDLINE
DOCUMENT NUMBER: 96261545 PubMed ID: 8777303
TITLE: One week treatment with omeprazole, clarithromycin and tinidazole or lansoprazole, amoxicillin and metronidazole for cure of Helicobacter pylori infection in duodenal ulcer patients.
AUTHOR: Sito E; Konturek P C; Bielanski W; Kwiecien N; Konturek S J; Baniukiewicz A; Jedynak M; Gabryelewicz A; Hahn E G
CORPORATE SOURCE: Institute of Physiology, Jagiellonan University School of Medicine, Cracow, Poland.
SOURCE: JOURNAL OF PHYSIOLOGY AND PHARMACOLOGY, (1996 Mar) 47 (1) 221-8.
Journal code: 9114501. ISSN: 0867-5910.

PUB. COUNTRY: Poland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199609
ENTRY DATE: Entered STN: 19960924
Last Updated on STN: 19990129
Entered Medline: 19960919

AB We defined optimal Helicobacter pylori (Hp) treatment as Hp eradication rate about 90%, well-tolerated with few side-effects. Two centers carried out randomized trials including 90 patients (74% men, 26% women, ages ranging from 18 to 65, mean age 42 +/- 8) with active duodenal ulcers (DU). Patients were treated with the ***combination*** of Omeprazole (O) 20 mg bd + Clarithromycin (C) 250 mg bd + Tinidazole (T) (500 mg bd) or with ***Lansoprazole*** (L) 15 mg bd + Amoxicillin (A) 750 mg bd + Metronidazole (M) 500 mg bd administered for one week. The DU healing rate was evaluated by endoscopy and the Hp status by rapid urease CLO-test and 14C-urea breath test (UBT). The healing rate of the DU in a group treated with the ***combination*** of O + C + T was 91% and in group treated with L + A + M was 93%. The eradication of Hp in group O + C + T and L + A + M averaged 91% and 87%, respectively. There was no statistically significant difference in the DU healing rate and the Hp eradication rate between these two groups. Both treatments were accompanied by a marked rise in the basal and postprandial plasma ***gastrin*** levels and the rise in the intragastric pH but these alterations returned to the pre-treatment values 4 weeks after the termination of the therapy. Both treatments were well tolerated and the only side effect was the taste disturbance observed in few patents treated with O + C + T. None of patients discontinued the treatment because of the adverse events. We conclude that one week treatment using O + C + T or L + A + M are highly and equally effective in the healing of DU and in the eradication of Hp.

L10 ANSWER 14 OF 33 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 96325611 MEDLINE
DOCUMENT NUMBER: 96325611 PubMed ID: 8661818
TITLE: Medical treatment of metastasizing carcinoid tumors.
AUTHOR: Arnold R
CORPORATE SOURCE: Department of Internal Medicine, Division of Gastroenterology and Metabolism, Philipps-University Marburg, Baldingerstrasse, D-35033 Marburg, Germany.
SOURCE: WORLD JOURNAL OF SURGERY, (1996 Feb) 20 (2) 203-7. Ref: 43
Journal code: 7704052. ISSN: 0364-2313.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961205

AB Long-acting somatostatin analogs, such as octreotide, comprise the therapeutic modality of choice for the symptomatic relief of flush and diarrhea in patients with carcinoid syndrome. The sequelae of gastric acid hypersecretion in patients with ***gastrin*** -producing duodenal carcinoids (gastrinoma) are perfectly controlled by ***proton*** ***pump*** ***inhibitors*** . Antiproliferative medical strategies to control the growth of metastatic carcinoid tumors include long-acting somatostatin analogs, interferon alpha, and the ***combination*** of the two. However, the success rate is less than 50%, and it is questionable whether true tumor regression can be expected. Controlled prospective studies are mandatory to address the question whether interferon or somatostatin analogs or the ***combination*** of the two should be used as first-line medical strategies and if hepatic artery embolization in patients with liver metastases should be performed before beginning medical therapy. Chemotherapy, including etoposide and cisplatin, has been shown to be effective only for purely differentiated neuroendocrine carcinomas and not for slowly growing carcinoids.

L10 ANSWER 15 OF 33 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 95121086 MEDLINE
DOCUMENT NUMBER: 95121086 PubMed ID: 7821104
TITLE: Effect of plaunotol on hypergastrinemia induced by

long-term omeprazole administration in humans.
AUTHOR: Kaneko H; Mit[redacted]a T; Nagai H; Harada M; Kotera[redacted] Furusawa A; Morise K
CORPORATE SOURCE: Fourth Department of Internal Medicine, Aichi Medical University, Japan.
SOURCE: DIGESTIVE DISEASES AND SCIENCES, (1995 Jan) 40 (1) 160-5.
Journal code: 7902782. ISSN: 0163-2116.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199502
ENTRY DATE: Entered STN: 19950223
Last Updated on STN: 19950223
Entered Medline: 19950214

AB Omeprazole markedly inhibits basal and stimulated gastric acid secretion and has the ability to produce hypergastrinemia and hyperplasia of enterochromaffin-like cells in humans. On the other hand, plaunotol, an acyclic diterpene alcohol, has been reported to inhibit ***gastrin*** release by stimulating endogenous secretion release. We investigated the effect of plaunotol on serum ***gastrin*** levels after six to eight weeks of omeprazole (20 mg/day) administration in 22 patients (16 males, 6 females; mean age 52.3, range 36-70 years) with peptic ulcer disease. The patients were randomized to the following two groups: 11 subjects with ***omerprazole*** alone (single group) and 11 with omeprazole plus plaunotol (240 mg/day) (***combination*** group) treatment. There were no significant differences between the two groups concerning age, sex, ulcer stage, ulcer history, environmental factors, and Helicobacter pylori (HP) prevalence. After complete drug(s) administration, serum immunoreactive (ir) - ***gastrin*** levels increased significantly in the single group ($P < 0.001$) in contrast to the ***combination*** group, and plaunotol significantly inhibited hypergastrinemia induced by omeprazole administration ($P < 0.001$). Significant increases in serum ir-calcitonin gene-related peptide concentrations were observed in the ***combination*** group compared to the single group ($P < 0.05$). However, there were no significant changes in sereum ir-secretin, somatostatin, and vasoactive intestinal polypeptide levels as well as ulcer healing and HP prevalence between the two groups. These findings suggest that plaunotol may suppress hypergastrinemia induced by long-term omeprazole administration, at least partly, via a certain brain-gut hormone affecting ***gastrin*** release.

L10 ANSWER 16 OF 33 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 96082617 MEDLINE
DOCUMENT NUMBER: 96082617 PubMed ID: 7594326
TITLE: Efficacy of lansoprazole and amoxicillin in eradicating Helicobacter pylori: evaluation using 13C-UBT and Monoclonal H. pylori antibody testing.
AUTHOR: Nakata H; Itoh H; Nishioka S
CORPORATE SOURCE: Second Department of Internal Medicine, Wakayama Medical College, Japan.
SOURCE: JOURNAL OF CLINICAL GASTROENTEROLOGY, (1995) 20 Suppl 2 S118-20.
Journal code: 7910017. ISSN: 0192-0790.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19990129
Entered Medline: 19951212

AB ***Combination*** therapy with ***lansoprazole*** (LPZ) and amoxicillin (AMPC) was administered to eradicate Helicobacter pylori. Changes in eradication rates were monitored and serum antibody titers, levels of pepsinogens I and II (PI and PII), and ***gastrin*** were measured. The 40 subjects were divided into two groups: one group received LPZ 30 mg alone, and the other received LPZ 30 mg and AMPC 1,500 mg concomitantly. AMPC was administered for 2 weeks before completion of LPZ treatment. Maintenance therapy was cimetidine 400 mg. The presence of H. pylori was evaluated using the urea breath test (UBT). The clearance rate was 12.5% and the eradication rate was 0% in the LPZ group, and the corresponding rates in the LPZ with AMPC group were 41.6 and

25.0%, respectively. Serum monoclonal H. pylori antibody titers decreased in patients in whom bacterial eradication had been achieved. Serum PI was significantly reduced in those patients in whom eradication had been achieved. Serum PII and ***gastrin*** levels also tended to decrease in patients in whom eradication had been achieved, but no such changes were observed in the other patients. Further research into drug treatment and evaluation methods for bacterial eradication is required.

L10 ANSWER 17 OF 33 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 96121787 MEDLINE
DOCUMENT NUMBER: 96121787 PubMed ID: 7495941
TITLE: No Helicobacter pylori, no Helicobacter pylori-associated peptic ulcer disease.
AUTHOR: Tytgat G N
CORPORATE SOURCE: Academic Medical Centre, Department of Gastroenterology & Hepatology, Amsterdam, The Netherlands.
SOURCE: ALIMENTARY PHARMACOLOGY AND THERAPEUTICS, (1995) 9 Suppl 1 39-42. Ref: 15
Journal code: 8707234. ISSN: 0269-2813.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960118
AB Virtually all duodenal ulcers (DUs) and the vast majority of gastric ulcers (GUs) are the consequence of Helicobacter pylori-associated inflammation. In DUs, the inflammation is maximal in the antrum and is associated with gastric metaplasia in the bulb. ***Gastrin*** homeostasis is disturbed by H. pylori gastritis and there is robust acid secretion. Successful eradication of the infection cures the ulcer diathesis. Amalgamated figures for ulcer relapse per year in H. pylori-positive DUs are > 60% compared with 2.6% for H. pylori-negative DU patients. The corresponding figures for GU are > 50% for H. pylori-positive and 2.0% for H. pylori-negative individuals. This striking difference in relapse rate persists, as the re-infection rate in the developed world is < 1% per year. Recurrent bleeding in bleeding-prone DUs is essentially abolished after cure of the infection. ***Proton*** ***pump*** ***inhibitors*** (PPIs) are increasingly used in eradication regimens. PPIs have intrinsic antimicrobial activity. MICs for ***lansoprazole*** (LAN) are lower than for omeprazole (OME). Two weeks of triple therapy (bismuth, tetracycline, imidazole) has, on average, a superior eradication efficacy (> or = 90%) compared with dual therapy (PPI, amoxycillin or clarithromycin) (> or = 80%). When a ***combination*** of PPI and two antibiotics has been used, results comparable to triple therapy have been reported. However, the side-effects profile and patient acceptability of PPI plus one or two antibiotic regimens are better than for traditional triple therapy.(ABSTRACT TRUNCATED AT 250 WORDS)

L10 ANSWER 18 OF 33 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 95091873 EMBASE
DOCUMENT NUMBER: 1995091873
TITLE: [Omeprazole and the new proton pump inhibitors].
OMEPRAZOL UND DIE NEUEN PROTONEN PUMPENHEMMER.
AUTHOR: Born P.; Classen M.
CORPORATE SOURCE: II. Medizinische Klinik, Klinikum Rechts der Isar, Technische Universitat, Ismaninger Strasse 22,D-81675 Munchen, Germany
SOURCE: Verdauungskrankheiten, (1995) 13/1 (23-31).
ISSN: 0174-738X CODEN: VERDEJ
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 048 Gastroenterology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: German
SUMMARY LANGUAGE: German; English
AB Omeprazole and the new ***proton*** ***pump*** ***inhibitors*** ***lansoprazole*** and ***pantoprazole*** , specific ***inhibitors*** of the H+/K+-ATPase in the parietal cells of the stomach suppress the gastric acid secretion in a way not reached before. Therefore, they are superior to H2-antagonists in the therapy of peptic

lesions like reflux oesophagitis, duodenal ulcer and Zollinger-Ellison syndrome. Although the importance of elevated levels of ***gastrin*** and the possible development of carcinoids is not definitively cleared, long-term treatment seems to be possible and should be able to prevent surgical intervention in special cases. Special importance ***proton*** ***pump*** ***inhibitors*** get in a ***combination*** therapy with antibiotics to eradicate helicobacter pylori.

L10 ANSWER 19 OF 33 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 95036730 MEDLINE
DOCUMENT NUMBER: 95036730 PubMed ID: 7949462
TITLE: Treatment of peptic ulcers from now to the millennium.
AUTHOR: Pounder R E
CORPORATE SOURCE: Royal Free Hospital and School of Medicine, London, UK.
SOURCE: BAILLIERES CLINICAL GASTROENTEROLOGY, (1994 Jun) 8 (2) 339-50. Ref: 61
Journal code: 8704786. ISSN: 0950-3528.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 19950110
Last Updated on STN: 19950110
Entered Medline: 19941208

AB The present strategies for the management of peptic ulceration are well tolerated and clinically effective. Histamine H2-receptor antagonists can be used for mild to moderate disease, and ***proton*** ***pump*** ***inhibitors*** are of particular benefit for patients with severe peptic ulceration and the Zollinger-Ellison syndrome. However, none of these treatments provides protection against recurrent ulceration, except when taken as long-term continuous treatment. Long-term exposure to pharmacological agents raises problems of safety, particularly relating to a lack of intragastric acidity. In addition, the accelerated development of atrophic gastritis in patients receiving omeprazole requires investigation and assessment. It is unlikely that there will be any major development in the area of control of gastric acid secretion, except perhaps the introduction of specific immunization against ***gastrin*** . However, the clinical benefit of this strategy awaits assessment. The main area for development must be the introduction of convenient and effective regimens for the eradication of Helicobacter pylori infection. Existing regimens are either simpler and relatively ineffective, or too complicated for widespread application. Bearing in mind the long gestation period of any new drug, it seems likely that the only innovative drug that will be introduced for the management of peptic ulceration before the millennium will be ranitidine bismuth citrate, an antisecretory anti-H. pylori drug that will usually be used in ***combination*** with an antibiotic.

L10 ANSWER 20 OF 33 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 95016101 MEDLINE
DOCUMENT NUMBER: 95016101 PubMed ID: 7523549
TITLE: A new CCK-B/gastrin receptor antagonist acts as an agonist on the rat pancreas.
AUTHOR: Koop I; Eissele R; Richter S; Patberg H; Meyer F; Mossner J; Arnold R; Koop H
CORPORATE SOURCE: Department of Internal Medicine, University of Marburg, Germany.
SOURCE: INTERNATIONAL JOURNAL OF PANCREATOLOGY, (1994 Jun) 15 (3) 215-22.
Journal code: 8703511. ISSN: 0169-4197.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19990129
Entered Medline: 19941121

AB The new CCK-B/ ***gastrin*** receptor antagonist PD 136450 is of potential value in treating neurologic and psychiatric disorders. We investigated possible side effects on the rat pancreas using acute and chronic administration schedules. In chronic experiments, four groups of rats were given either PD 136450, the ***proton*** ***pump*** ***inhibitor*** BY 308 (in order to induce hypergastrinemia), a

combination of both or control solutions over 14 d. Pancreatic growth, DNA, and protein content were significantly increased in rats given PD 136450 irrespective of circulating ***gastrin*** levels. Furthermore, an anticoordinate shift in pancreatic enzyme content in favor of trypsin and chymotrypsin at the expense of amylase and lipase was observed. Plasma CCK levels remained unchanged in this group making a role of circulating hormone unlikely. In order to investigate a possible direct agonist effect of the CCK-B/ ***gastrin*** receptor antagonist, we studied amylase release from isolated rat pancreatic acini in response to PD 136450 and sulfated CCK8 alone and in ***combination*** with the specific CCK-A receptor antagonist MK 329. Increasing concentrations of PD 136450 caused a monophasic dose-response curve in contrast to the well-known biphasic amylase release in response to CCK8. Addition of increasing doses of PD 136450 to a concentration of CCK causing maximal stimulation of amylase release (0.1 nM) further enhanced amylase release from pancreatic acini. The specific CCK-A receptor antagonist MK 329 dose-dependently ***inhibited*** CCK8- and PD 136450-induced amylase release. In conclusion, the new CCK-B/ ***gastrin*** receptor antagonist PD 136450 exhibited profound agonist actions on the rat pancreas mediated via CCK-A receptors.

L10 ANSWER 21 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:284343 BIOSIS
DOCUMENT NUMBER: PREV199497297343
TITLE: An anti- ***gastrin*** effect of enprostil or pirenzepine in ***combination*** with ***proton*** ***pump*** ***inhibitor*** in rats.
AUTHOR(S): Takiuchi, H.; Asada, S.; Ashida, K.; Umegaki, E.; Tahashi, T.; Ohshiba, S.
CORPORATE SOURCE: 2nd Dep. Internal Med., Osaka Med. Coll., Takatuki, Osaka Japan
SOURCE: Gastroenterology, (1994) Vol. 106, No. 4 SUPPL., pp. A193.
Meeting Info.: 95th Annual Meeting of the American Gastroenterological Association New Orleans, Louisiana, USA May 15-18, 1994
ISSN: 0016-5085.
DOCUMENT TYPE: Conference
LANGUAGE: English

L10 ANSWER 22 OF 33 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 95005335 MEDLINE
DOCUMENT NUMBER: 95005335 PubMed ID: 7921145
TITLE: Hp and pH--the relevance of gastric acid to the treatment of Helicobacter pylori infection.
AUTHOR: Hunt R H
CORPORATE SOURCE: Division of Gastroenterology, McMaster University, Hamilton, Ontario, Canada.
SOURCE: JOURNAL OF GASTROENTEROLOGY, (1994 Jul) 29 Suppl 7 128-33.
Ref: 43
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19990129
Entered Medline: 19941121

AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosa, which results in a disturbance of the regulation of ***gastrin*** , gastric acid, and pepsin secretion. Acid secretion may be diminished, normal, or increased, depending on the stage of H. pylori infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known, but probably involve the release of cytokines in response to bacterial products initiating mucosal inflammation. Helicobacter pylori is suppressed, although not eradicated, by ***proton*** ***pump*** ***inhibitors*** . In various dose ***combinations*** with amoxycillin, omeprazole in a twice daily dose of up to 40 mg b.i.d. eradicates the organism in up to 82% of patients. This synergistic effect may be due to the direct effects of omeprazole, the protection of amoxycillin from acid degradation, or the enhancement of host defense mechanisms accompanying acid suppression.

L10 ANSWER 23 OF 33 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 96050259 MEDLINE
DOCUMENT NUMBER: 96050259 PubMed ID: 7502535
TITLE: Gastric acid secretion: activation and inhibition.
AUTHOR: Sachs G; Prinz C; Loo D; Bamberg K; Besancon M; Shin J M
CORPORATE SOURCE: University of California Los Angeles, USA.
CONTRACT NUMBER: RO1 DK 40165 (NIDDK)
RO1 DK 43301 (NIDDK)
SOURCE: YALE JOURNAL OF BIOLOGY AND MEDICINE, (1994 May-Aug) 67 (3-4) 81-95. Ref: 68
Journal code: 0417414. ISSN: 0044-0086.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
ENTRY DATE: Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960116

AB Peripheral regulation of gastric acid secretion is initiated by the release of ***gastrin*** from the G cell. ***Gastrin*** then stimulates the cholecystokinin-B receptor on the enterochromaffin-like cell beginning a calcium signaling cascade. An exocytotic release of histamine follows with concomitant activation of a Cl- current. The released histamine begins the H2-receptor mediated sequence of events in the parietal cell, which results in activation of the gastric H+/K+ - ATPase. This enzyme is the final common pathway of acid secretion. The H+/K+ - ATPase is composed of two subunits: the larger alpha-subunit couples ion transport to hydrolysis of ATP, the smaller beta-subunit is required for appropriate assembly of the holoenzyme. Both the membrane and extracytoplasmic domain contain the ion transport pathway, and therefore, this region is the target for the antisecretory drugs of the post-H2 era. The 100 kDa alpha-subunit has probably 10 membrane spanning segments with, therefore, five extracytoplasmic loops. The 35 kDA beta-subunit has a single membrane spanning segment, and most of this protein is extracytoplasmic with the six or seven N glycosylation consensus sequences occupied. Omeprazole is an acid-accumulated, acid-activated, prodrug that binds covalently to two cysteine residues at positions 813 (or 822) and 892, accessible from the acidic face of the pump. ***Lansoprazole*** binds to cys321, 813 (or 822) and 892; ***pantoprazole*** binds to cys813 and 822. The common binding site for these drugs (cys813 or 822) is responsible for the inhibition of acid transport. Covalent inhibition of the acid pump improves control of acid secretion, but since the effective half life of the inhibition in man is about 48 hr, full inhibition of acid secretion, perhaps necessary for eradication of Helicobacter pylori in ***combination*** with a single antibiotic, will require prolongation of the effect of this class of drug.

L10 ANSWER 24 OF 33 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 94254616 MEDLINE
DOCUMENT NUMBER: 94254616 PubMed ID: 8196467
TITLE: [Lansoprazole--profile of a new proton pump inhibitor].
Lansoprazol--Profil eines neuen Protonenpumpenhemmers.
AUTHOR: Seifert E
CORPORATE SOURCE: I. Med. Klinik, Stadt. Krankenhaus Kemperhof Koblenz.
SOURCE: LEBER, MAGEN, DARM, (1994 Mar) 24 (2) 66-8, 71. Ref: 27
Journal code: 0311747. ISSN: 0300-8622.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940707
Last Updated on STN: 19940707
Entered Medline: 19940627

AB ***Lansoprazole*** , a new ***proton*** ***pump*** ***inhibitor*** , selectively ***inhibits*** the H+/K(+)-ATPase. Its ***inhibitory*** effect on basal and ***gastrin*** stimulated gastric acid secretion is equal to omeprazole and stronger than that of H2-receptor antagonists. Healing rates concerning gastric and duodenal ulcers and refluxesophagitis are significantly higher compared to H2-receptor antagonists and at least comparable to omeprazole. Regarding pilot studies in H. pylori eradication therapy, ***lansoprazole*** in ***combination*** with various antibiotics is expected to show good

eradication rates. Considering its excellent safety and interaction profile ***lansoprazole*** is effective and safe in treating acid related disorders.

L10 ANSWER 25 OF 33 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 94:624411 SCISEARCH
THE GENUINE ARTICLE: NE188
TITLE: LANSOPRAZOLE - PROFILE OF A NEW PROTON PUMP INHIBITOR
AUTHOR: SEIFERT E (Reprint)
CORPORATE SOURCE: STADT KRANKENHAUS KEMPERHOF, MED KLIN 1, KOBLENZER STR 115, D-56073 KOBLENZ, GERMANY (Reprint)
COUNTRY OF AUTHOR: GERMANY
SOURCE: LEBER MAGEN DARM, (MAR 1994) Vol. 24, No. 2, pp. 66. ISSN: 0300-8622.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: CLIN
LANGUAGE: German
REFERENCE COUNT: No References Keyed
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB E. Seifert. Koblenz (Germany): ***Lansoprazole*** - profile of a new ***proton*** ***pump*** ***inhibitor*** ***Lansoprazole*** , a new ***proton*** ***pump*** ***inhibitor*** . selectively ***inhibits*** the H+/K+-ATPase. Its ***inhibitory*** effect on basal and ***gastrin*** stimulated gastric acid secretion is equal to omeprazole and stronger than that of H-2-receptor antagonists. Healing rates concerning gastric and duodenal ulcers and refluxesophagitis are significantly higher compared to H-2-receptor antagonists and at least comparable to omeprazole. Regarding pilot studys in H. pylori eradication therapy, ***lansoprazole*** in ***combination*** with various antibiotics is expected to show good eradication rates.

Considering its excellent safety and interaction profile lansoprazole is effective and safe in treating acid related disorders.

L10 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1993:574209 CAPLUS
DOCUMENT NUMBER: 119:174209
TITLE: Therapeutic combinations of gastrin antagonists and ATPase inhibitors for the treatment of peptic disorders
INVENTOR(S): Horwell, David Christopher; Hunter, John Cureton
PATENT ASSIGNEE(S): Warner-Lambert Co., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9312817	A1	19930708	WO 1992-US10692	19921211
W: AU, CA, JP, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9332475	A1	19930728	AU 1993-32475	19921211

PRIORITY APPLN. INFO.: US 1991-811487 19911220
WO 1992-US10692 19921211

AB ***Combinations*** of ***proton*** ***pump*** ***inhibitors*** and CCK-B/ ***gastrin*** antagonists are effective in the treatment of peptic disorders, such as ulcers and gastroesophageal reflux disease and in the treatment of Zollinger-Ellison syndrome. Pharmacol. effects of [R-[R*, S*-(E)]]-4-[[2-[[3-(1H-indol-3-yl)-2-methyl-1-oxo-2-[[(tricyclo[3.3.1.13,7]dec-2-yloxy)carbonylamino]propylamino]-3-phenylpropylamino-4-oxo-2-butenoic acid as ***gastrin*** antagonist in ***combination*** with BY 308 as ATPase ***inhibitor*** were tested with rats.

L10 ANSWER 27 OF 33 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 17
ACCESSION NUMBER: 94004911 EMBASE
DOCUMENT NUMBER: 1994004911
TITLE: [Hp and pH: Implications for the eradication of Helicobacter pylori].
HP ET PH: IMPLICATIONS POUR L'ERADICATION DE HELICOBACTER PYLORI.
AUTHOR: Hunt R.H.
CORPORATE SOURCE: 4W8E Health Sciences Centre, McMaster University Medical

Centre, 1200 Main Street West,Hamilton, Ont. L8N 3Z5, Canada
SOURCE: Canadian Journal of Gastroenterology, (1993) 7/3 SUPPL. (406-410).
ISSN: 0835-7900 CODEN: CJGAEJ
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosae, which results in a disturbance of the regulatory mechanisms for ***gastrin*** , gastric acid and pepsin secretion. Acid secretion may by decreased, normal or increased, depending on the stage of infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known but may be due to the release of cytokines in response to bacterial toxins. H pylori colonization os reduced by effective acid suppression with ***proton*** ***pump*** ***inhibitors*** , although it is not eradicated. In ***combination*** with amoxycillin, omeprazole, up to 40 mg twice daily, eradicated the organism in up to 82% of cases. This synergistic effect may be due for a direct effect of omeprazole on the organism, the protection of amoxycillin from acid degradation, or enhancement of host defence mechanisms accompanying acid suppression.

L10 ANSWER 28 OF 33 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 93257561 MEDLINE
DOCUMENT NUMBER: 93257561 PubMed ID: 8490076
TITLE: Proton pump inhibitors, enterochromaffin-like cell growth and Helicobacter pylori gastritis.
AUTHOR: Solcia E; Villani L; Luinetti O; Fiocca R
CORPORATE SOURCE: Department of Human Pathology and Genetics, University of Pavia, Italy.
SOURCE: ALIMENTARY PHARMACOLOGY AND THERAPEUTICS, (1993) 7 Suppl 1 25-8, discussion 29-31. Ref: 38
Journal code: 8707234. ISSN: 0269-2813.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 19930625
Last Updated on STN: 19930625
Entered Medline: 19930617
AB In both rodents and humans the development of ***gastrin*** -promoted gastric argyrophil enterochromaffin-like cell carcinoids requires the involvement of a genetic factor inherent to multiple endocrine neoplasia syndrome or of type A autoimmune chronic atrophic gastritis. Prolonged severe hypergastrinaemia acting on non-gastritic mucosa, as in Zollinger-Ellison syndrome patients, results in diffuse argyrophil enterochromaffin-like cell hyperplasia but, as a rule, does not produce tumours. ***Combination*** of chronic atrophic gastritis (mostly related to Helicobacter pylori infection) with hypergastrinaemia frequently causes linear and micronodular hyperplasia of argyrophil cells, whereas carcinoids are exceptional. No tumours or pre-neoplastic lesions have been observed in patients treated long-term with ***proton*** ***pump*** ***inhibitors*** , apart from rare cases in patients with combined Zollinger-Ellison and multiple endocrine neoplasia syndromes. A moderate increase in the incidence of argyrophil cell clustering, with or without hyperplasia, probably results from the parallel evolution of ulcer-associated Helicobacter gastritis into chronic atrophic gastritis. Eradication of H. pylori with a ***combination*** of ***proton*** ***pump*** ***inhibitors*** and antibiotics suppresses gastritis and prevents ulcer recurrence.

L10 ANSWER 29 OF 33 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 93109619 EMBASE
DOCUMENT NUMBER: 1993109619
TITLE: Proton pump inhibitors, enterochromaffin-like growth and Helicobacter pylori gastritis.
AUTHOR: Solcia E.; Villani L.; Luinetti O.; Fiocca R.
CORPORATE SOURCE: Sezione di Anatomia Patiologica, Dipartimento Patol. Umana

Ereditaria, Universita degli Studi di Pavia, Via Forlanini n.16,27100 Pavia, Italy
SOURCE: Alimentary Pharmacology and Therapeutics, Supplement, (1993) 7/1 (25-28).
ISSN: 0953-0673 CODEN: ATSLEO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In both rodents and humans the development of ***gastrin*** -promoted gastric argyrophil enterochromaffin-like cell carcinoids requires the involvement of a genetic factor inherent to multiple endocrine neoplasia syndrome or of type A autoimmune chronic atrophic gastritis. Prolonged severe hypergastrinaemia acting on non-gastritic mucosa, as in Zollinger-Ellison syndrome patients, results in diffuse argyrophil enterochromaffin-like cell hyperplasia but, as a rule, does not produce tumours. ***Combination*** of chronic atrophic gastritis (mostly related to Helicobacter pylori infection) with hypergastrinaemia frequently causes linear and micronodular hyperplasia of argyrophil cells, whereas carcinoids are exceptional. No tumours or pre-neoplastic lesions have been observed in patients treated long-term with ***proton*** ***pump*** ***inhibitors*** , apart from rare cases in patients with combined Zollinger-Ellison and multiple endocrine neoplasia syndromes. A moderate increase in the incidence of argyrophil cell clustering, with or without hyperplasia, probably results from the parallel evolution of ulcer-associated. Helicobacter gastritis into chronic atrophic gastritis. Eradication of H. pylori with a ***combination*** of ***proton*** ***pump*** ***inhibitors*** and antibiotics suppresses gastritis and prevents ulcer recurrence.

L10 ANSWER 30 OF 33 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
DUPLICATE 19
ACCESSION NUMBER: 93175441 EMBASE
DOCUMENT NUMBER: 1993175441
TITLE: Hp and pH: Implications for the eradication of Helicobacter pylori.
AUTHOR: Hunt R.H.
CORPORATE SOURCE: Division of Gastroenterology, McMaster University Medical Centre, 1200 Main Street West,Hamilton, Ont. L8N 3Z5, Canada
SOURCE: Scandinavian Journal of Gastroenterology, Supplement, (1993) 28/196 (12-16).
ISSN: 0085-5928 CODEN: SJGSB8
COUNTRY: Norway
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosae, which results in a disturbance of the regulatory mechanisms for ***gastrin*** , gastric acid and pepsin secretion. Acid secretion may be decreased, normal or increased, depending on the stage of infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known but may be due to the release of cytokines in response to bacterial toxins. H. pylori colonization is reduced by effective acid suppression with ***proton*** ***pump*** ***inhibitors*** , although it is not eradicated. In ***combination*** with amoxycillin, omeprazole, up to 40 mg twice daily, eradicated the organism in up to 82% of cases. This synergistic effect may be due to a direct effect of omeprazole on the organism, the protection of amoxycillin from acid degradation, or enhancement of host defence mechanisms accompanying acid suppression.

L10 ANSWER 31 OF 33 MEDLINE on STN
ACCESSION NUMBER: 93342443 MEDLINE
DOCUMENT NUMBER: 93342443 PubMed ID: 8341986
TITLE: Hp and pH: implications for the eradication of Helicobacter pylori.
AUTHOR: Hunt R H

CORPORATE SOURCE: Division of Gastroenterology, McMaster University, Hamilton, Ontario, Canada.
SOURCE: SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY. SUPPLEMENT, (1993) 196 12-6. Ref: 42
Journal code: 0437034. ISSN: 0085-5928.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930917
Last Updated on STN: 19930917
Entered Medline: 19930831

AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosae, which results in a disturbance of the regulatory mechanisms for ***gastrin*** , gastric acid and pepsin secretion. Acid secretion may be decreased, normal or increased, depending on the stage of infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known but may be due to the release of cytokines in response to bacterial toxins. H. pylori colonization is reduced by effective acid suppression with ***proton*** ***pump*** ***inhibitors*** , although it is not eradicated. In ***combination*** with amoxycillin, omeprazole, up to 40 mg twice daily, eradicated the organism in up to 82% of cases. This synergistic effect may be due to a direct effect of omeprazole on the organism, the protection of amoxycillin from acid degradation, or enhancement of host defence mechanisms accompanying acid suppression.

L10 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:401398 CAPLUS
DOCUMENT NUMBER: 117:1398
TITLE: Effect of acute and chronic acid suppression on plasma gastrin release in the rat
AUTHOR(S): Schuerer-Maly, C. C.; Kromer, W.; Flogerzi, B.; Varga, L.; Postius, S.; Halter, F.
CORPORATE SOURCE: Gastrointest. Unit, Univ. Bern, Bern, CH-3010, Switz.
SOURCE: Alimentary Pharmacology and Therapeutics (1992), 6(2), 196-206
CODEN: APTHEN; ISSN: 0269-2813
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mechanisms possibly involved in the interaction of antral pH and hypergastrinemia were investigated using various ***combinations*** of the ***proton*** ***pump*** ***inhibitor*** B 831-78, a substituted benzimidazole with irreversible action like omeprazole, antimuscarinic drugs, and modification of antral pH. Interruption of the neg. feedback between gastric acidity and ***gastrin*** release may be directly responsible for hypergastrinemia induced by H+, K+-ATPase ***inhibition*** in rats.

L10 ANSWER 33 OF 33 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:451302 BIOSIS
DOCUMENT NUMBER: PREV199598465602
TITLE: Gastric acid secretion: Activation and inhibition.
AUTHOR(S): Sachs, George (1); Prinz, Christian; Loo, Don; Bamberg, Krister; Besancon, Marie; Shin, Jai Moo
CORPORATE SOURCE: (1) Room 324, Build. 113, Wadsworth VA Hosp., Los Angeles, CA 90073 USA
SOURCE: Yale Journal of Biology and Medicine, Vol. 67, No. 3-4, pp. 81-95.
ISSN: 0044-0086.
DOCUMENT TYPE: General Review
LANGUAGE: English

AB Peripheral regulation of gastric acid secretion is initiated by the release of ***gastrin*** from the G cell. ***Gastrin*** then stimulates the cholecystokinin-B receptor on the enterochromaffin-like cell beginning a calcium signaling cascade. An exocytotic release of histamine follows with concomitant activation of a Cl- current. The released histamine begins the H-2-receptor mediated sequence of events in the parietal cell, which results in activation of the gastric H+/K+-ATPase. This enzyme is the final common pathway of acid secretion. The H+/K+-ATPase is composed of two subunits: the larger alpha-subunit couples ion transport to hydrolysis of ATP, the smaller alpha-subunit is required for appropriate assembly of the holoenzyme. Both the membrane and extracytoplasmic domain contain the ion transport pathway, and therefore,

this region is the target for the antisecretory drugs of the post-H-2 era. The 100 kDa alpha-subunit has probably 10 membrane spanning segments with, therefore, five extracytoplasmic loops. The 35 kDA beta-subunit has a single membrane spanning segment, and most of this protein is extracytoplasmic with the six or seven N glycosylation consensus sequences occupied. Omeprazole is an acid-accumulated, acid-activated, prodrug that binds covalently to two cysteine residues at positions 813 (or 822) and 892, accessible from the acidic face of the pump. ***Lansoprazole*** binds to cys321, 813 (or 822) and 892; ***pantoprazole*** binds to cys813 and 822. The common binding site for these drugs (cys813 or 822) is responsible for the inhibition of acid transport. Covalent inhibition of the acid pump improves control of acid secretion, but since the effective half life of the inhibition in man is about 48 hr, full inhibition of acid secretion, perhaps necessary for eradication of Helicobacter pylori in ***combination*** with a single antibiotic, will require prolongation of the effect of this class of drug.

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=> d his

     (FILE 'HOME' ENTERED AT 08:00:39 ON 14 AUG 2003)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     08:01:08 ON 14 AUG 2003
L1         83063 S PENTAGASTRIN OR GASTRIN
L2             0 S PROTEON PUMP
L3         28429 S PROTON PUMP
L4         17931 S L3 (P) INHIBIT?
L5           893 S L1 (P) L4
L6         10766 S RABEPRAZOLE OR OMERPRAZOLE OR LANSOPRAZOLE OR PANTOPRAZOLE
L7           698 S L1 (P) L6
L8          1268 S L5 OR L7
L9            75 S L8 (P) (COMBINAT? OR CONJUNCT? OR ADUNCT?)
L10           33 DUPLICATE REMOVE L9 (42 DUPLICATES REMOVED)

=> s l8 (p) synergis?
L11            9 L8 (P) SYNERGIS?

=> duplicate remove l11
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L11
L12            5 DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED)

=> d l12 1-5 ibib abs

L12  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2001:247197  CAPLUS
DOCUMENT NUMBER:          134:247252
TITLE:                    Use of pentagastrin to inhibit gastric acid secretion
                          or as a diuretic
INVENTOR(S):              Pisegna, Joseph R.; Wank, Stephen
PATENT ASSIGNEE(S):       The Regents of the University of California, USA
SOURCE:                   PCT Int. Appl., 42 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001022985      A1   20010405       WO 2000-US26992  20000928
     WO 2001022985      C2   20020926
         W:  CA, JP
         RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE
PRIORITY APPLN. INFO.:                    US 1999-156491P  P  19990928
                                          US 2000-671764   A  20000927
AB     ***Pentagastrin*** , when administered in conjunction with a
       ***proton***  ***pump***  ***inhibitor***  (PPI), is
       ***synergistic*** with the PPI and significantly increases the efficacy
     of the PPI in reducing/mitigating excess gastric acid secretion.
REFERENCE COUNT:          4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12  ANSWER 2 OF 5     MEDLINE on STN                    DUPLICATE 1
```

ACCESSION NUMBER: 95005335 MEDLINE
DOCUMENT NUMBER: 95005335 PubMed ID: 7921145
TITLE: Hp and pH--the relevance of gastric acid to the treatment of Helicobacter pylori infection.
AUTHOR: Hunt R H
CORPORATE SOURCE: Division of Gastroenterology, McMaster University, Hamilton, Ontario, Canada.
SOURCE: JOURNAL OF GASTROENTEROLOGY, (1994 Jul) 29 Suppl 7 128-33. Ref: 43
Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19990129
Entered Medline: 19941121

AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosa, which results in a disturbance of the regulation of ***gastrin*** , gastric acid, and pepsin secretion. Acid secretion may be diminished, normal, or increased, depending on the stage of H. pylori infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known, but probably involve the release of cytokines in response to bacterial products initiating mucosal inflammation. Helicobacter pylori is suppressed, although not eradicated, by ***proton*** ***pump*** ***inhibitors*** . In various dose combinations with amoxycillin, omeprazole in a twice daily dose of up to 40 mg b.i.d. eradicates the organism in up to 82% of patients. This ***synergistic*** effect may be due to the direct effects of omeprazole, the protection of amoxycillin from acid degradation, or the enhancement of host defense mechanisms accompanying acid suppression.

L12 ANSWER 3 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN DUPLICATE 2
ACCESSION NUMBER: 94004911 EMBASE
DOCUMENT NUMBER: 1994004911
TITLE: [Hp and pH: Implications for the eradication of Helicobacter pylori].
HP ET PH: IMPLICATIONS POUR L'ERADICATION DE HELICOBACTER PYLORI.
AUTHOR: Hunt R.H.
CORPORATE SOURCE: 4W8E Health Sciences Centre, McMaster University Medical Centre, 1200 Main Street West,Hamilton, Ont. L8N 3Z5, Canada
SOURCE: Canadian Journal of Gastroenterology, (1993) 7/5 SUPPL. (406-410).
ISSN: 0835-7900 CODEN: CJGAEJ
COUNTRY: Canada
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English; French

AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosae, which results in a disturbance of the regulatory mechanisms for ***gastrin*** , gastric acid and pepsin secretion. Acid secretion may by decreased, normal or increased, depending on the stage of infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known but may be due to the release of cytokines in response to bacterial toxins. H pylori colonization os reduced by effective acid suppression with ***proton*** ***pump*** ***inhibitors*** , although it is not eradicated. In combination with amoxycillin, omeprazole, up to 40 mg twice daily, eradicated the organism in up to 82% of cases. This ***synergistic*** effect may be due for a direct effect of omeprazole on the organism, the protection of amoxycillin from acid degradation, or enhancement of host defence mechanisms accompanying acid suppression.

L12 ANSWER 4 OF 5 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN DUPLICATE 3
ACCESSION NUMBER: 93175441 EMBASE

DOCUMENT NUMBER: 1993175441
TITLE: Hp and pH: Implications for the eradication of Helicobacter pylori.
AUTHOR: Hunt R.H.
CORPORATE SOURCE: Division of Gastroenterology, McMaster University Medical Centre, 1200 Main Street West,Hamilton, Ont. L8N 3Z5, Canada
SOURCE: Scandinavian Journal of Gastroenterology, Supplement, (1993) 28/196 (12-16).
ISSN: 0085-5928 CODEN: SJGSB8
COUNTRY: Norway
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
048 Gastroenterology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosae, which results in a disturbance of the regulatory mechanisms for ***gastrin*** , gastric acid and pepsin secretion. Acid secretion may be decreased, normal or increased, depending on the stage of infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known but may be due to the release of cytokines in response to bacterial toxins. H. pylori colonization is reduced by effective acid suppression with ***proton*** ***pump*** ***inhibitors*** , although it is not eradicated. In combination with amoxycillin, omeprazole, up to 40 mg twice daily, eradicated the organism in up to 82% of cases. This ***synergistic*** effect may be due to a direct effect of omeprazole on the organism, the protection of amoxycillin from acid degradation, or enhancement of host defence mechanisms accompanying acid suppression.

L12 ANSWER 5 OF 5 MEDLINE on STN
ACCESSION NUMBER: 93342443 MEDLINE
DOCUMENT NUMBER: 93342443 PubMed ID: 8341986
TITLE: Hp and pH: implications for the eradication of Helicobacter pylori.
AUTHOR: Hunt R H
CORPORATE SOURCE: Division of Gastroenterology, McMaster University, Hamilton, Ontario, Canada.
SOURCE: SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY. SUPPLEMENT, (1993) 196 12-6. Ref: 42
Journal code: 0437034. ISSN: 0085-5928.
PUB. COUNTRY: Norway
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 19930917
Last Updated on STN: 19930917
Entered Medline: 19930831
AB Helicobacter pylori infection causes inflammation of the gastric and duodenal mucosae, which results in a disturbance of the regulatory mechanisms for ***gastrin*** , gastric acid and pepsin secretion. Acid secretion may be decreased, normal or increased, depending on the stage of infection, although the meal-stimulated ***gastrin*** response is invariably elevated. The exact mechanisms involved are not known but may be due to the release of cytokines in response to bacterial toxins. H. pylori colonization is reduced by effective acid suppression with ***proton*** ***pump*** ***inhibitors*** , although it is not eradicated. In combination with amoxycillin, omeprazole, up to 40 mg twice daily, eradicated the organism in up to 82% of cases. This ***synergistic*** effect may be due to a direct effect of omeprazole on the organism, the protection of amoxycillin from acid degradation, or enhancement of host defence mechanisms accompanying acid suppression.

=> d his

(FILE 'HOME' ENTERED AT 08:00:39 ON 14 AUG 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 08:01:08 ON 14 AUG 2003

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L1        83063 S PENTAGASTRIN OR [redacted]ASTRIN
L2            0 S PROTEON PUMP
L3        28429 S PROTON PUMP
L4        17931 S L3 (P) INHIBIT?
L5          893 S L1 (P) L4
L6        10766 S RABEPRAZOLE OR OMERPRAZOLE OR LANSOPRAZOLE OR PANTOPRAZOLE
L7          698 S L1 (P) L6
L8         1268 S L5 OR L7
L9           75 S L8 (P) (COMBINAT? OR CONJUNCT? OR ADUNCT?)
L10          33 DUPLICATE REMOVE L9 (42 DUPLICATES REMOVED)
L11           9 S L8 (P) SYNERGIS?
L12           5 DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED)

=> s (gastric acid secretion) or (zollinger syndrome) or (ellison syndrome) or (gastroesophageal r
   4 FILES SEARCHED...
L13       46626 (GASTRIC ACID SECRETION) OR (ZOLLINGER SYNDROME) OR (ELLISON
                SYNDROME) OR (GASTROESOPHAGEAL REFLUX DISEASE) OR (PEPTITIC
                ULCER DISEASE)

=> s (peptic ulcer disease) or (atrophic gastritis) or esophagitis or (idiopathic gastric acid hyp
L14       52382 (PEPTIC ULCER DISEASE) OR (ATROPHIC GASTRITIS) OR ESOPHAGITIS
                OR (IDIOPATHIC GASTRIC ACID HYPERSECRETION)

=> s l13 or l14
L15       93120 L13 OR L14

=> s l8 (p) l15
L16         511 L8 (P) L15

=> s l16 (p) (COMBINAT? OR CONJUNCT? OR ADUNCT? or synergis)
L17          25 L16 (P) (COMBINAT? OR CONJUNCT? OR ADUNCT? OR SYNERGIS)

=> duplicate remove l17
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L17
L18          13 DUPLICATE REMOVE L17 (12 DUPLICATES REMOVED)

=> s l18 not (l10 or l12)
L19           0 L18 NOT (L10 OR L12)

=> s antibiotic or penicillin or tetracyclin or macrolide or cephalosporin or fluoroguinone
L20      951066 ANTIBIOTIC OR PENICILLIN OR TETRACYCLIN OR MACROLIDE OR CEPHALOS
                PORIN OR FLUOROGUINONE

=> s (l10 or l12) (p) l20
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L148) (P) L136'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L154) (P) L138'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L157) (P) L139'
L21          11 (L10 OR L12) (P) L20

=> s pisegna joseph/au
L22          11 PISEGNA JOSEPH/AU

=> s wank stephen/au
L23           5 WANK STEPHEN/AU

=> s (l22 or l23) and l8
L24           1 (L22 OR L23) AND L8

=> d l24 1 ibib abs

L24  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2001:247197  CAPLUS
DOCUMENT NUMBER:          134:247252
TITLE:                    Use of pentagastrin to inhibit gastric acid secretion
                          or as a diuretic
INVENTOR(S):              Pisegna, Joseph R.;   ***Wank, Stephen***
PATENT ASSIGNEE(S):       The Regents of the University of California, USA
SOURCE:                   PCT Int. Appl., 42 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022985	A1	20010405	WO 2000-US26992	20000928
WO 2001022985	C2	20020926		

W: CA, JP
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-156491P P 19990928
US 2000-671764 A 20000927

AB ***Pentagastrin*** , when administered in conjunction with a ***proton*** ***pump*** ***inhibitor*** (PPI), is synergistic with the PPI and significantly increases the efficacy of the PPI in reducing/mitigating excess gastric acid secretion.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 08:00:39 ON 14 AUG 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 08:01:08 ON 14 AUG 2003

```
L1        83063 S PENTAGASTRIN OR GASTRIN
L2            0 S PROTEON PUMP
L3        28429 S PROTON PUMP
L4        17931 S L3 (P) INHIBIT?
L5          893 S L1 (P) L4
L6        10766 S RABEPRAZOLE OR OMERPRAZOLE OR LANSOPRAZOLE OR PANTOPRAZOLE
L7          698 S L1 (P) L6
L8         1268 S L5 OR L7
L9           75 S L8 (P) (COMBINAT? OR CONJUNCT? OR ADUNCT?)
L10          33 DUPLICATE REMOVE L9 (42 DUPLICATES REMOVED)
L11           9 S L8 (P) SYNERGIS?
L12           5 DUPLICATE REMOVE L11 (4 DUPLICATES REMOVED)
L13       46626 S (GASTRIC ACID SECRETION) OR (ZOLLINGER SYNDROME) OR (ELLISON
L14       52382 S (PEPTIC ULCER DISEASE) OR (ATROPHIC GASTRITIS) OR ESOPHAGITIS
L15       93120 S L13 OR L14
L16         511 S L8 (P) L15
L17          25 S L16 (P) (COMBINAT? OR CONJUNCT? OR ADUNCT? OR SYNERGIS)
L18          13 DUPLICATE REMOVE L17 (12 DUPLICATES REMOVED)
L19           0 S L18 NOT (L10 OR L12)
L20      951066 S ANTIBIOTIC OR PENICILLIN OR TETRACYCLIN OR MACROLIDE OR CEPHA
L21          11 S (L10 OR L12) (P) L20
L22          11 S PISEGNA JOSEPH/AU
L23           5 S WANK STEPHEN/AU
L24           1 S (L22 OR L23) AND L8
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=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.38	155.59
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.91	-3.91

STN INTERNATIONAL LOGOFF AT 08:17:51 ON 14 AUG 2003